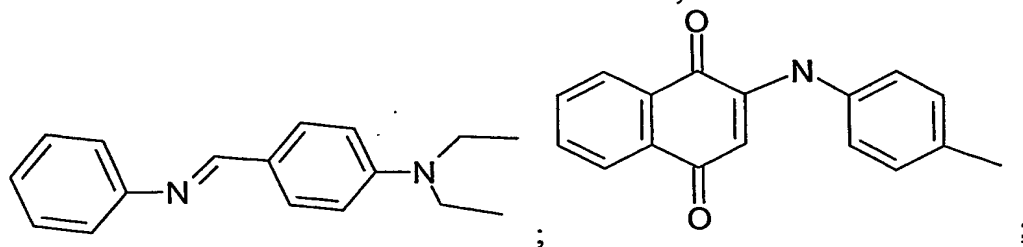
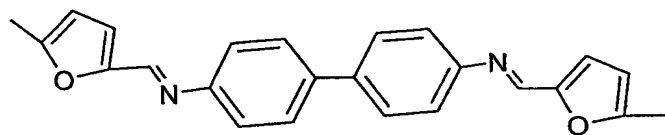
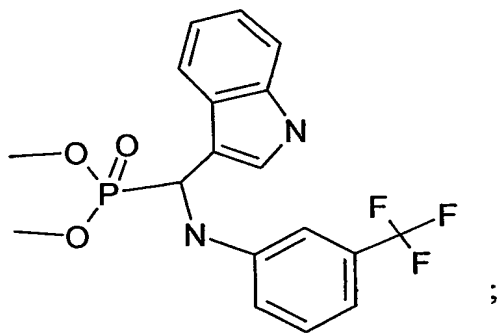
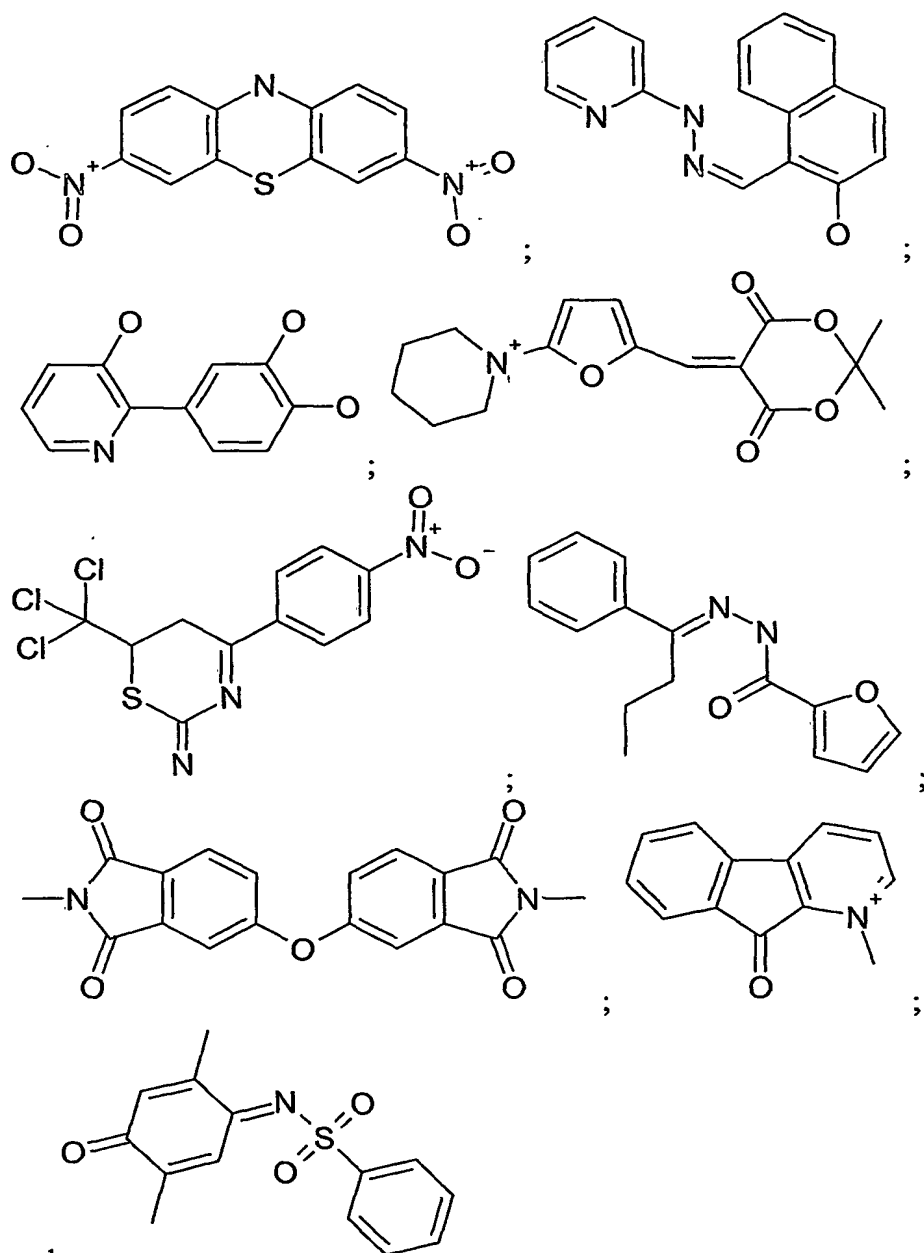


What is claimed is:

1. An isolated, purified or recombinant complex, comprising a Cbl-b polypeptide and a POSH polypeptide.
2. An isolated, purified or recombinant complex, comprising
 - a) a Cbl-b polypeptide; and
 - b) a polypeptide comprising a domain that is at least 90% identical to a POSH SH3 domain.
3. A method of identifying an antiviral agent, comprising identifying a test agent that disrupts a complex of any of claims 1-2.
4. The complex of any of claims 1-2, wherein the Cbl-b polypeptide is a human Cbl-b polypeptide.
5. The complex of any of claims 1-2, wherein the POSH polypeptide is a human POSH polypeptide.
6. A method of identifying an agent that modulates an activity of a Cbl-b polypeptide and a POSH polypeptide, comprising identifying an agent that disrupts a complex of any one of claims 1-2, wherein an agent that disrupts a complex of any one of claims 1-2 is an agent that modulates an activity of the Cbl-b polypeptide or the POSH polypeptide.
7. A method of identifying an antiviral agent, comprising:
 - a) identifying a test agent that disrupts a complex comprising a Cbl-b polypeptide and a Cbl-b-AP polypeptide; and
 - b) evaluating the effect of the test agent on a function of a virus, wherein an agent that inhibits a pro-infective or pro-replicative function of a virus is an antiviral agent.
8. The method of claim 7, wherein the Cbl-b-AP is POSH.
9. The method of claim 7, wherein the virus is an envelope virus.
10. The method of claim 9, wherein the virus is a Human Immunodeficiency Virus.
11. The method of claim 7, wherein evaluating the effect of the test agent on a function of the virus comprises evaluating the effect of the test agent on the budding, release, infectivity, or reverse transcriptase activity of the virus or a virus-like particle.
12. A method of treating a viral infection in a subject in need thereof, comprising administering, in an amount sufficient to inhibit the viral infection, an agent that inhibits the expression of or an activity of a Cbl-b polypeptide.

13. The method of claim 12, wherein said agent is selected from among: an siRNA construct, an antisense construct, an antibody, a polypeptide, and a small molecule.
- 5 14. The method of claim 13, wherein the agent is an siRNA construct comprising a nucleic acid sequence that hybridizes to an mRNA encoding a Cbl-b polypeptide.
- 10 15. The method of claim 14, wherein the siRNA construct inhibits the expression of a Cbl-b polypeptide.
16. The method of claim 15, wherein the siRNA construct is selected from among SEQ ID NOS: 59-64.
- 15 17. The method of claim 13, wherein the agent is a small molecule selected from among:





18. The method of claim 17, wherein the small molecule inhibits the ubiquitin
ligase activity of a Cbl-b polypeptide.

19. The method of claim 12, wherein the subject is infected with an envelope
virus.

20. The method of claim 19, wherein the envelope virus is a Human
Immunodeficiency Virus.

21. Use of an inhibitor of Cbl-b for the manufacture of a medicament for treatment of a viral infection.
- 5 22. A packaged pharmaceutical for use in treating a viral infection, comprising:
a) a pharmaceutical composition comprising an inhibitor of a Cbl-b polypeptide and a pharmaceutically acceptable carrier; and
b) instructions for use.
- 10 23. The method of claim 22, wherein the viral infection is caused by an envelope virus.
24. The method of claim 23, wherein the virus is a Human Immunodeficiency Virus.
- 15 25. A method of identifying an antiviral agent, comprising:
a) identifying a test agent that inhibits an activity of or expression of a Cbl-b polypeptide; and
b) evaluating an effect of the test agent on a function of a virus.
- 20 26. A method of evaluating an antiviral agent, comprising:
a) providing a test agent that inhibits an activity of or expression of a Cbl-b polypeptide; and
b) evaluating an effect of the test agent on a function of a virus.
- 25 27. The method of claim 25 or 26, wherein the virus is an envelope virus.
28. The method of claim 25 or 26, wherein the virus is a Human Immunodeficiency Virus.
- 30 29. The method of claim 25 or 26, wherein evaluating the effect of the test agent on a function of the virus comprises evaluating the effect of the test agent on the budding, release, infectivity, or reverse transcriptase activity of the virus or a virus-like particle.
- 35 30. The method of claim 25 or 26, wherein the test agent is selected from among: an siRNA construct, an antisense construct, an antibody, a polypeptide, and a small molecule.
- 40 31. The method of claim 30, wherein the test agent is an siRNA construct that inhibits the expression of Cbl-b and is selected from among SEQ ID NOS: 59-64.
- 45 32. A method of identifying an agent that modulates a Cbl-b function, comprising:
a) identifying an agent that modulates a POSH polypeptide; and
b) testing the effect of the agent on a Cbl-b function.

33. A method of evaluating an agent that modulates a Cbl-b function, comprising:
a) providing an agent that modulates a POSH polypeptide; and
b) testing the effect of the agent on a Cbl-b function.
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34. The method of claim 32 or 33, wherein testing the effect of the agent on a Cbl-b function comprises contacting a cell with the agent and measuring the effect of the agent on Cbl-b-mediated ubiquitination.
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35. The method of claim 32 or 33, wherein testing the effect of the agent on a Cbl-b function comprises contacting a cell with the agent and measuring the effect of the agent on the budding, release, infectivity, or reverse transcriptase activity of a virus or a virus-like particle.
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36. A method of identifying an agent that modulates a POSH function, comprising:
a) identifying an agent that modulates a Cbl-b polypeptide; and
b) testing the effect of the agent on a POSH function.
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37. A method of evaluating an agent that modulates a POSH function, comprising:
a) providing an agent that modulates a Cbl-b polypeptide; and
b) testing the effect of the agent on a POSH function.
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38. The method of claim 36 or 37, wherein testing the effect of the agent on a POSH function comprises contacting a cell with the agent and measuring the effect of the agent on POSH-mediated ubiquitination.
- 30
39. A method of identifying an antiviral agent, comprising:
a) forming a mixture comprising a Cbl-b polypeptide, ubiquitin, and a test agent; and
b) detecting the ubiquitin ligase activity of the Cbl-b polypeptide, wherein an agent that inhibits the ubiquitin ligase activity of the Cbl-b polypeptide, is an antiviral agent.
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40. A method of identifying an antiviral agent, comprising:
a) providing a Cbl-b polypeptide and a test agent; and
b) identifying a test agent that binds to the Cbl-b polypeptide.
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41. A method of identifying an agent with antiviral activity, comprising:
a) contacting a Cbl-b polypeptide with a test agent; and
b) identifying a test agent that inhibits a Cbl-b activity.
- 45
42. A method of identifying an antiviral agent, comprising:
a) providing a Cbl-b polypeptide and a test agent; and
b) identifying a test agent that interacts with the Cbl-b polypeptide.

43. The method of any of claims 40-42, further comprising evaluating the effect of the test agent on Cbl-b mediated ubiquitination.
- 5 44. The method of any of claims 40-42, further comprising evaluating the effect of the test agent on the budding, release, infectivity, or reverse transcriptase activity of a virus or a virus-like particle..
- 10 45. A method of inhibiting a viral infection, comprising administering an agent to a subject in need thereof, wherein said agent inhibits the interaction between a Cbl-b polypeptide and a POSH polypeptide.
- 15 46. A method of inhibiting a viral infection, comprising administering to a subject in need thereof, an agent that inhibits the expression of or an activity of a Cbl-b polypeptide, wherein said agent inhibits the expression of or an activity of the Cbl-b polypeptide.
- 20 47. The method of claim 46, wherein the agent inhibits the ubiquitin ligase activity of the Cbl-b polypeptide.
- 25 48. An isolated Cbl-b nucleic acid comprising a nucleic acid sequence at least 85% identical to the nucleic acid sequence depicted in SEQ ID NO: 43.
49. The isolated Cbl-b nucleic acid of claim 48, wherein the nucleic acid comprises the nucleic acid sequence depicted in SEQ ID NO: 43.
- 30 50. An isolated Cbl-b polypeptide, comprising the amino acid sequence depicted in SEQ ID NO: 45.
51. An isolated Cbl-b nucleic acid comprising a nucleic acid sequence at least 85% identical to the nucleic acid sequence depicted in SEQ ID NO: 44.
- 35 52. The isolated Cbl-b nucleic acid of claim 51, wherein the nucleic acid comprises the nucleic acid sequence depicted in SEQ ID NO: 44.
53. An isolated Cbl-b polypeptide, comprising the amino acid sequence depicted in SEQ ID NO: 46.
- 40 54. A method of identifying an anti-apoptotic agent, comprising:
a) identifying a test agent that disrupts a complex comprising a Cbl-b polypeptide and a POSH polypeptide; and
b) evaluating the effect of the test agent on apoptosis of a cell, wherein an agent that decreases apoptosis of the cell is an anti-apoptotic agent.
- 45 55. A method of identifying an anti-cancer agent, comprising:
a) identifying a test agent that disrupts a complex comprising a Cbl-b polypeptide and a POSH polypeptide; and

b) evaluating the effect of the test agent on proliferation or survival of a cancer cell,
wherein an agent that decreases proliferation or survival of a cancer cell is an anti-cancer agent.

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56. The method of claim 54, wherein the cancer cell is a cell derived from a POSH-associated cancer.

57. A method of identifying an agent that inhibits the progression of a neurological disorder, comprising:

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- a) identifying a test agent that disrupts a complex comprising a Cbl-b polypeptide and a Cbl-b-AP polypeptide; and
- b) evaluating the effect of the test agent on the trafficking of a protein through the secretory pathway,

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wherein an agent that disrupts localization of a Cbl-b-AP polypeptide is an agent that inhibits progression of a neurological disorder.

58. The method of claim 57, wherein the Cbl-b-AP is POSH.

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59. The method of claim 57, wherein the Cbl-b-AP is a POSH-AP.

60. A method of identifying an agent that inhibits the progression of a neurological disorder, comprising:

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- a) identifying a test agent that disrupts a complex comprising a Cbl-polypeptide and a POSH polypeptide; and
- b) evaluating the effect of the test agent on the ubiquitination of a protein.

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61. A method of treating or preventing a POSH-associated cancer in a subject comprising administering an agent that inhibits the expression of or an activity of a Cbl-b polypeptide to a subject in need thereof, wherein said agent treats or prevents the POSH-associated cancer.

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62. A method of treating or preventing a POSH-associated neurological disorder in a subject comprising administering an agent that inhibits the expression of or an activity of a Cbl-b polypeptide to a subject in need thereof, wherein said agent treats or prevents the POSH-associated neurological disorder.

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63. A method of treating or preventing a POSH-associated viral disorder in a subject comprising administering an agent that inhibits the expression of or an activity of a Cbl-b polypeptide to a subject in need thereof, wherein said agent treats or prevents the POSH-associated viral disorder.

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